REMARKS

Claims 1-17 and 19-22 were pending. Claims 6-9 and 16 have been cancelled. Claims 4, 10-12, 14 and 17 have been amended. Therefore, claims 1-5, 10-15, 17, and 19-22 will be pending upon entry of this amendment.

No new matter has been added. Claims 4, 10, 11, and 12 have been amended to clarify the invention. Support for the amendments to claim 14 can be found, for example, at least at page 9, lines 17-26 of the specification as originally filed. Support for the amendments to claim 17 can be found, for example, in the claims as originally filed.

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

Rejection of Claims 14-17 and 19 under 35 U.S.C. § 112, first paragraph

Claims 14-17 and 19 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner alleges that the "specification, while being enabling for a method of treating a proliferative disorder of the type disclosed in Table 3 does not reasonably provide enablement for a method of treating proliferative disorders generally.

Applicants respectfully disagree with the Examiner's assessment that the specification does not reasonably provide enablement for treatment of the proliferative disorders claimed in the present application, other than disorders of the type disclosed in Table 3. However, in the interests of expediency, claim 14 has been amended to recite that the method is for treating a CDK-sensitive or CDK-dependent proliferative disorder.

In light of this limitation and based on the teachings provided in Applicants' specification, Applicants respectfully submit that no undue experimentation would be required in order to carry out the methods of the present invention. By way of illustration, Example 19 describes detailed experimental protocols by which the kinase specifity of a selected compound may be assayed. Thus, assays for CDK4/Cyclin D1, CDK2/Cyclin E, CDIK1/Cyclin B kinase may be carried out by monitoring the phosphorylation of GST-Rb. Alternatively, a CDK2/Cyclin A kinase assay can be conducted using purified histone H1 and for CDK4 using recombinant GST-retinoblastoma protein. In addition, Example 19 also discloses a suitable assay for the determination of PKCα kinase activity.

Furthermore, Example 20 provides the methodology for assessing the presently claimed compounds in a standard cellular proliferation assay using human tissue cell lines. In this regard, Table 1 provides data comparing the CDK2/E and CDK4/D1 kinase inhibition of the compounds, along with their anti-proliferative activity in a cytotoxicity assay using A549 (lung cancer), HT29 (colon cancer), and Saos-2 (bone osteosarcoma) cell lines. In addition, Table 3 details the *in vitro* anti-proliferative activity of representative compounds, in particular, compounds [10] and [16]. As the Examiner will appreciate, numerous (25) proliferative cell lines were assessed.

With regard to the Examiner's opinion that tumor progression involves multiple mechanisms and that there is no single therapeutic approach in existence for the treatment of all tumors, Applicants respectfully submit that the skilled artisan would be able to determine which CDK sensitive or dependent proliferative disorders could be treated with the antiproliferative compounds of the present invention. It is disclosed in the specification that "an anti-proliferative effect within the scope of the present invention may be demonstrated by the ability to inhibit cell proliferation in an *in vitro* whole cell assay, for example using any of the cell lines A549, HT29, Saos-2, HeLa or MCF-7, or by showing inhibition of a CDK enzyme (such as CDK2 or CDK4) in an appropriate assay" (page 8, lines 15-19). Both of these assays have been exemplified in the present case.

In respect to Blain and Lu Valle, Applicants respectfully submit that the cited sentences do not controvert Applicants' assertions. Blain is directed specifically to the differential interaction of a particular cyclin dependent kinase inhibitor $p27^{Kip1}$ with Cyclin A-Cdk2 and Cyclin D2-Cdk4. Lu Valle is a general review article about cell cycle control in growth plate chondocytes. Neither of the articles controvert Applicants' assertions, e.g., that the compounds of the invention are useful for treating CDK sensitive or dependent proliferative disorders. It is Applicants' understanding that the disclosure of the invention set forth by Applicants in their application must be given the presumption of correctness and operativeness by the PTO, and the only relevant concern of the PTO under the circumstances should concern the truth of the assertions contained in the application. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1967); see also, *In re Bowen*, 492 F.2d 859, 181 U.S.P.Q. 48 (C.C.P.A. 1974). Applicants submit that the Examiner offers nothing in the instant Office Action to controvert the truth of Applicants' assertions in the instant application, e.g., that the claimed compounds are useful for treating CDK-sensitive and dependent disorders..

Therefore, Applicants respectfully submit that determining which CDK-sensitive or CDK-dependent proliferative disorder may be treated by the compounds of the present invention would not present an undue burden to the skilled artisan. Applicants respectfully request that this rejection of claims 14-17 and 19 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejection of Claims 1-17 and 19-22 under Judicially Created Doctrine of Obviousness Type Double Patenting

Claims 1-17 and 19-22 are rejected on the grounds of obviousness type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,531,479. In particular, the Examiner is of the opinion that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because instantly claimed compounds are encompassed by [the] genus of the reference."

While in no way admitting that Claims 1-17 and 19-22 are obvious over claims 1-23 of U.S. Patent No. 6,818,634, upon allowance of the present application but for the obviousness type double patenting rejection, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

Rejection of Claim 4 under 35 U.S.C. § 112, second paragraph

Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter.

In particular, claim 4 was rejected for lacking proper antecedent basis. Applicants respectfully submit that this rejection no longer pertains to the claim as currently amended.

Duplicate Claims

Claims 6, 8, and 9 were rejected as being substantial duplicates of claims 1, 3, and 4. Applicants disagree. However, in the interest of expediting prosecution, Applicants have cancelled claims 6, 8, and 9, thus rendering the rejection of these claims moot.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephonic conference with Applicant's Attorney would be helpful in expediting the prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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